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Regional and social inequalities in chronic renal replacement therapy in Denmark

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Abstract

Background. The incidence of chronic renal replacement therapy (RRT) varies markedly between Danish nephrology centres. The aim of the present study was to establish if there is regional and social variation in the incidence of chronic RRT in Denmark when analysed according to patient residence. The importance of diabetic nephropathy and patients aged 70 years or older was also studied.

Methods. Incident patients on chronic RRT in the period 1995–2006 were identified in the Danish National Registry on Regular Dialysis and Transplantation. Information on residence, income, educational status and ethnic origin was obtained from Statistics Denmark. Rates of incident RRT patients were standardized for regional differences of sex and age as well as income, educational status and ethnic origin. Poisson regression was used when comparing rates.

Results. Age- and sex-standardized incident chronic RRT rates among individuals with low income or short educational level were higher (P < 0.0001) compared to other groups. Also, standardized rates of patients in total and patients aged 70 years or older were higher in the catchment areas of the nephrology centres located in the two largest cities than for patients with residence in other areas of the country (P < 0.0001). Standardizing for regional differences of ethnic origin did not change the rates. The incident chronic RRT rate caused by diabetic nephropathy was higher for patients with residence in the catchment area of the nephrology centre in the largest city [49 per million people (p.m.p.) (95% CI = 40–57 p.m.p.)] compared to the catchment area of the nephrology centre located in the second largest city [31 (95% CI = 26–37 p.m.p.)] and other areas [29 p.m.p. (95% CI = 26–31 p.m.p.)] in 2001–06. When standardizing for differences in income among the 30–69-year-old persons, the rate of patients with residence in the catchment area of the nephrology centre located in the largest city decreased but was still higher than in other regions (P = 0.0003).

Conclusions. There are marked socio-economic and regional differences in rates of incident RRT patients. The rates of incident RRT patients are highest in the catchment areas of the two largest nephrology centres and this may be partly explained by a higher frequency of end-stage diabetic nephropathy and a new treatment programme targeting frail, mainly elderly, patients.

Keywords: demographic factors; diabetic end-stage renal disease; regional differences; renal replacement therapy; socio-economic factors

Introduction

The overall incidence of chronic renal replacement therapy (RRT) in Denmark doubled during the decade 1991 to 2001, from 70 to 138 per million people (p.m.p.). Since then, it has stabilized or even tended to decrease to a level around 120 p.m.p. [1]. It is generally taken that the increase is caused by a less restrictive treatment strategy and a high patient acceptance of RRT despite old age and comorbidity. The decrease might have been partly due to a reduction in the number of patients with diabetic nephropathy [1,2]. During the whole period, there have
been marked differences in the incidence of RRT between dialysis centres [1]. It is known that some patients are treated outside their local centre, but this probably only partly explains the variation in the incidence of RRT. Regional differences may suggest the presence of factors controllable by better prevention and treatment of diabetes and chronic kidney disease (CKD). Previous studies have reported regional differences in RRT [3–7] and regional variation in the prevalence of diabetes has been suggested as a reason [8].

In cardiac disease, socio-economic differences in the treatment after acute myocardial infarction have been shown [9,10]. An inverse relationship between socio-economic status and rates of incident RRT patients has been described in CKD, with higher rates in the socio-economically disadvantaged group [11–13].

The aim of the present study was to establish if there is regional and social variation in the incidence of chronic RRT in Denmark when analysed according to patient residence and standardized for demographic factors. The importance of diabetic nephropathy and patients aged 70 years or older was also studied.

Materials and methods

The Danish population and health care system

The Danish population consisted of 5.2 million persons in 1995, increasing to 5.4 in 2006 [14]. Approximately 20% of the population live in the two largest city areas of central Copenhagen (Copenhagen and Frederiksberg municipalities) and Aarhus (including suburbs and surrounding municipalities, until 1 January 2007 called Aarhus County) with ~0.6 million persons in each. They represent the catchment areas of the two largest nephrology centres in Denmark. Immigrants and descendants accounted for 5% of the total population in 1995 and 9% in 2006 with ~2:3 of these originating from non-Western countries [14].

Denmark has a tax-financed universal health care system with free access for all citizens to hospitals and essential operations. During the period, the number of dialysis centres was 15 (one centre was opened and one closed). No private dialysis centres exist. For various reasons, such as complications related to initiation of dialysis, severe comorbidity or limited local dialysis capacity, some patients are treated outside their local dialysis centre.

Data sources and definitions

Chronic renal replacement therapy Data on onset of chronic RRT and renal diagnosis were obtained from The Danish National Registry on Regular Dialysis and Transplantation [1] where all patients actively treated for end-stage CKD are registered. Once a year, all regional centres refer data to a central database at the national registry. Identical software is used. One specific nephrologist in each of all regional nephrology centres in Denmark is responsible for referring the data. Data are based on medical records and, for incident patients, the registration includes age, sex, renal diagnosis, treatment modality and dialysis centre. The material is checked for internal consistency and appropriate corrections are made in agreement with the reporting centres. Only patients with at least 3 months need of RRT are included in the registry, thereby excluding acute renal failure. A recent validation study of the registry has shown that completeness of incident patient registration was highly acceptable with no regional variation. Validity of incident patient data was also high, except for the type of diabetes [15].

Patient residence Data on patient residence the year RRT was initiated were obtained from Statistics Denmark [14] and, if missing, were found in the Danish Civil Registration System.

Regions The age- and sex-standardized rates of incident RRT patients (1995–2006) resident in 13 counties outside the catchment areas of the two largest nephrology centres located in Copenhagen and Aarhus County showed no significant differences. Therefore, in the following analyses, we compared the rates of patients resident in three regions: Copenhagen, Aarhus County (Aarhus) and the rest of the country.

Income and education Information on income and highest level of completed education was also obtained from Statistics Denmark. Income was defined as total income in the year 5 years before the start of RRT including transfer payments, business profits and pensions, with the exception of private pensions. Income was corrected for inflation according to the price index in Statistics Denmark. Lastly, income was grouped into low, medium and high income corresponding to the level of 33.7% of the Danish population aged 30–69 years with the lowest income in 2006, 38.0% with medium income and 28.3% with the highest income. Patients were divided into three groups according to the highest level of completed education: (i) primary school, (ii) high school and skilled labour and (iii) persons with university degrees, nurses, librarians, physiotherapists, school teachers, etc. [14]. Patients with missing information on educational status (4.6% of the 30–69-year-old persons) were excluded.

Ethnic origin Ethnic origin was defined according to the patients’ and their parents’ country of birth and citizenship with (i) immigrants, being persons born outside Denmark with both parents also born abroad or both with non-Danish citizenship; (ii) descendants, being persons born in Denmark whose parents do not have Danish citizenship and are not born in Denmark; and (iii) Danes, being persons with at least one parent having Danish citizenship and being born in Denmark [14]. Origin was divided into Danish and, for immigrants and descendants, into Western and non-Western. Countries of the EU, Andorra, Australia, Canada, Iceland, Monaco, New Zealand, Norway, San Marino, Switzerland, USA and the Vatican State were defined as Western countries. Non-Western countries were defined as those not being Western countries or Denmark [16].

Supplementary analyses

(i) Aarhus County was broken up into the high population-dense area of Aarhus Municipality and the rest of Aarhus County as well as Copenhagen compared to the rest of Denmark. (ii) One-year mortality in the three regions was compared.

Patient population

The patient population consisted of all patients starting chronic RRT from 1995 to 2000 and 2001 to 2006 in Denmark, with the exception of patients from Greenland and the Faroe Islands. Patients without residence permit were not included.

Statistics

Patients were classified according to place of residence irrespective of which nephrology centre in which they initiated RRT in. All analyses were adjusted according to the underlying population in each region and adjusted for gender and age using 5-year age bands. Furthermore, they were standardized for the highest level of completed education, alternating income and ethnic origin. All rates were standardized using the direct method. The Danish 2006 population was used as standard population [14] so that differences in age groups, gender, income, education and origin in the analysed regions were taken into consideration. Poisson regression was used when analysing differences in the incidence rates between regions, groups of income, level of education and groups of origin. We used the Kruskal–Wallis test to compare mean ages in the three regions.

Cox proportional hazards model, with time to death as outcome variable, was used to estimate the relative risk of mortality within 365 days in patients resident in Aarhus, Copenhagen and other regions of Denmark. Adjustment was made for regional differences of age, sex and immigration within 1 year.

Results

A total of 7636 patients initiated chronic RRT from 1 January 1995 to 31 December 2006 in Denmark. The number of new RRT patients was 193 residing in Copenhagen,
1025 in Aarhus and 5698 in other regions (Table 1). The proportion of women was stable at 37–39%.

The mean age of incident RRT patients was 60.3 years (range 0–89 years) in those residing in Copenhagen, 62.5 years (range 5–92 years) in Aarhus and 59.5 years (range 0–92 years) in other regions of Denmark. The mean age in Aarhus was significantly higher compared to Copenhagen and other regions (P < 0.0001). The mean age increased during the period from 54.6 years (range 0–85 years) in 1995 to 61.9 years (range 0–87 years) in 2001 and 62.7 years (range 1–92 years) in 2006. The change in mean age over the 12-year period was significant (P < 0.0001) (Figure 1).

The proportion of patients aged 70 years or more was significantly higher for patients residing in Copenhagen and Aarhus than in other regions of Denmark and increased from 34 and 32%, respectively, in 1995–2000 to 39 and 45% in 2001–06. The increase from the first to the second period was significant for Aarhus and other regions (P < 0.0001). The proportion of female patients aged 70 years or older was 37% in total but higher in Copenhagen (44%) compared to Aarhus (41%) and other regions (35%). The proportion of the population aged 70 years or more was stable in Denmark in total (11%) and Aarhus (10%) from 1995 to 2006, while decreasing in Copenhagen from 14 to 9% [14]. In the period 1995–2000, there was no difference in the proportion of patients with diabetic nephropathy starting chronic RRT between the three regions, whereas in 2001–06, there was a higher proportion of patients with diabetic nephropathy starting chronic RRT in Copenhagen (28%) compared to patients residing in Aarhus (20%) and other regions (24%). During the whole period, Copenhagen had a higher proportion of patients with low income compared to Aarhus and patients resident in other regions. The proportion of incident RRT patients with no other education than primary school was lower in patients residing in Copenhagen compared to Aarhus and other regions of Denmark.

The proportion of immigrants and descendants among new RRT patients was higher in Copenhagen (14–16%) than in the rest of the country (5–7%).

Incidence of RRT patients in different groups of income and education

The age- and sex-standardized rates of incident RRT among patients aged 30–69 years were significantly higher among individuals with low income or short education in 1995–2000 and in 2001–06 compared to the rates among persons with medium income or medium education. In contrast, the rates were lower among individuals with high income or long education compared to medium income or medium education (Figure 2).

Incidence of RRT patients in different groups of ethnic origin

There were no significant differences between the age- and sex-standardized rates of incident RRT patients in groups of different ethnic origin in 1995–2000, whereas 2001–06 showed a significant difference with higher rates in individuals with non-Western origin (184 p.m.p.) compared to Danish origin (126 p.m.p.) and Western origin (134 p.m.p.) (P < 0.0001) (Table 2).

Regional variation in incidence of renal replacement therapy patients

When standardized for regional differences of sex and age composition in the population, the incident chronic RRT patient rates in the period from 1995 to 2000 were significant-

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**Table 1.** Basic characteristics of incident RRT patients in three regions of Denmark from 1995 to 2006

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Copenhagen</td>
<td>Aarhus</td>
</tr>
<tr>
<td>Number of incident RRT patients</td>
<td>456</td>
<td>439</td>
</tr>
<tr>
<td>Mean age (range)</td>
<td>(4–87)</td>
<td>(7–87)</td>
</tr>
<tr>
<td>Patients ≥70 years (%)</td>
<td>34</td>
<td>32</td>
</tr>
<tr>
<td>Incident RRT in diabetic nephropathy (%)</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Patients with low income (30–69 years) (%)</td>
<td>69</td>
<td>56</td>
</tr>
<tr>
<td>Patients with only primary school (30–69 years) (%)</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Immigrants and descendants from non-Western countries (%)</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

Diabetes (ICD-10 E10-E14).
Low income: ≤5%0 200 €/year (33.7% of the Danes with the lowest income in 2006, corrected for inflation).
Western countries: Andorra, Australia, Canada, EU, Iceland, Monaco, New Zealand, Norway, San Marino, Switzerland, USA and the Vatican State.
Non-Western countries: those not being Western countries or Denmark.

...
ly higher in Copenhagen and Aarhus than the rates of patients residing in other regions of the country (160 and 115 p.m.p. versus 101 p.m.p., respectively) (P < 0.0001).

Also, the incident chronic RRT patient rates in the period from 2001 to 2006 were significantly higher in Copenhagen (164 p.m.p.) and Aarhus (156 p.m.p.) compared to other regions of the country (120 p.m.p.) (P < 0.001). There was a marked increase in rates of patients resident in Aarhus and other regions from 1995–2000 to 2001–06, while the rate of patients resident in Copenhagen remained stable (Figure 3).

The rates did not change significantly when standardized for regional differences in ethnic origin (Table 3).

The age- and sex-standardized rates of incident RRT patients aged 70 years or more were significantly higher in Copenhagen (562 p.m.p.) (P < 0.0001) and Aarhus (363 p.m.p.) (P < 0.003) compared to the rates of patients resident in other regions of Denmark (245 p.m.p.) in 1995–2000 and in Copenhagen (642 p.m.p.) and Aarhus (687 p.m.p.) in 2001–06 (P < 0.0001). There was a marked rise in rates of patients aged 70 years or more in all three regions from 1995–2000 to 2001–06, although to a lesser extent in Copenhagen.

The standardized rates of patients with diabetic nephropathy starting chronic RRT did not differ significantly between regions during 1995–2000 with 31 p.m.p. in Copenhagen, 24 p.m.p. in Aarhus and 23 p.m.p. in other regions. During 2001–06, the standardized rate of patients with diabetic nephropathy starting chronic RRT was significantly higher in Copenhagen (49 p.m.p.) compared to rates of patients residing in other regions of Denmark (29 p.m.p.) and Aarhus (31 p.m.p.) (P < 0.0001) (Table 3). There was an increase in rates of patients with diabetic nephropathy in Copenhagen from 1995–2000 to 2001–06.

The rate of incident RRT patients among 30–69-year-old persons was significantly higher in Copenhagen (174 p.m.p.) compared to rates of those resident in other regions (126 p.m.p.) in 1995–2000 (P < 0.0001). When standardized for regional differences in income, the rate of patients resident in Copenhagen decreased but was still significantly higher than the rate in other regions of Denmark (P = 0.002). Standardizing for regional differences of educational level increased the rates of Copenhagen and Aarhus to be both significantly higher than the rate in other regions (P = 0.0006 and P = 0.04). The results for the period 2001–06 were similar (Table 4). There was an increase in rates of 30–69-year-old persons resident in Aarhus and other regions from 1995–2000 to 2001–06, while the rate in Copenhagen remained stable.

Supplementary analyses

Rates of incident RRT patients resident in high- and low-density population areas of Aarhus County. The rate in Aarhus Municipality [124 p.m.p. (95% CI = 106–142)] as

Table 2. Rates and rate ratios (RR) of incident RRT patients in three groups of origin in Denmark 1995–2006, standardized for age and sex

<table>
<thead>
<tr>
<th></th>
<th>Danish origin</th>
<th>Western origin</th>
<th>Non-Western origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995–2000 RRT rates and RR standardized for age and sex (95% CI)</td>
<td>Rate RR</td>
<td>Rate RR</td>
<td>Rate RR</td>
</tr>
<tr>
<td></td>
<td>106 (102–110) 1.00</td>
<td>120 (95–144) 1.13 (0.94–1.37)</td>
<td>124 (97–152) 1.06 (0.89–1.26)</td>
</tr>
<tr>
<td>2001–06 RRT rates and RR standardized for age and sex (95% CI)</td>
<td>Rate RR</td>
<td>Rate RR</td>
<td>Rate RR</td>
</tr>
<tr>
<td></td>
<td>126 (122–130) 1.00</td>
<td>134 (107–161) 1.01 (0.84–1.23)</td>
<td>184 (150–218)* 1.47 (1.26–1.71)*</td>
</tr>
</tbody>
</table>

*P < 0.0001.
Western origin: persons originating from Andorra, Australia, Canada, EU, Iceland, Monaco, New Zealand, Norway, Switzerland, Vatican State and USA.
well as Copenhagen [160 p.m.p. (95% CI = 145–175)] differed from the rest of the country [101 p.m.p. (95% CI = 97–104)] in 1995–2000, in contrast to the rate in the rest of Aarhus County [114 p.m.p. (95% CI = 100–128)]. In 2001–06, the rates rose in the rest of Aarhus County to 150 p.m.p. (95% CI = 134–166) and differed significantly, as well as the rate in Aarhus Municipality [175 p.m.p. (95% CI = 153–197)] and Copenhagen [164 p.m.p. (95% CI = 148–179)], from the rest of Denmark [120 p.m.p. (95% CI = 116–124)].

Regional 1-year mortality in incident RRT patients. Of the incident RRT patients, 19–20% died within 365 days, irrespective of region of residence. Time to death within 1 year did not differ between Copenhagen, Aarhus or other regions when adjusted for regional differences of age and sex.

Discussion

The present study shows that, in the period 1995–2006, there were significantly higher rates of incident chronic RRT patients among persons with low income or short education compared to other groups. Furthermore, the incident RRT rates of patients resident in the catchment areas of the two largest Danish nephrology centres located in central Copenhagen and Aarhus were significantly higher when standardized for age and sex differences compared to rates of patients resident in other regions of Denmark even after controlling for differences of ethnic origin. There were significantly higher rates of incident RRT patients aged 70 years or more resident in Copenhagen and Aarhus compared to other regions and, furthermore, there was a marked rise in rates of patients aged 70 years or older resident in Aarhus from 1995–2000 to 2001–06.

Table 3. Rates and RR of incident RRT patients in three different regions of Denmark 1995–2000 and 2001–06, standardized for age, sex and origin

<table>
<thead>
<tr>
<th></th>
<th>Copenhagen</th>
<th>Aarhus</th>
<th>Other regions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate (95% CI)</td>
<td>Rate (95% CI)</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>1995–2000 RRT rates and RR standardized for age and sex (95% CI)</td>
<td>160 (145–175)*</td>
<td>115 (104–126)*</td>
<td>101 (97–105)</td>
</tr>
<tr>
<td></td>
<td>1.50 (1.36–1.66)*</td>
<td>1.13 (1.02–1.25)*</td>
<td>1.00</td>
</tr>
<tr>
<td>2001–06 RRT rates and RR standardized for age and sex (95% CI)</td>
<td>164 (148–179)*</td>
<td>156 (143–168)*</td>
<td>120 (116–124)</td>
</tr>
<tr>
<td></td>
<td>1.32 (1.19–1.45)*</td>
<td>1.28 (1.17–1.40)*</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*P < 0.05 when compared with other regions.

Diabetes (ICD-10 E10-E14).

Western countries: Andorra, Australia, Canada, EU, Iceland, Monaco, New Zealand, Norway, San Marino, Switzerland, USA and the Vatican State.
Table 4. Rates and RR of incident RRT patients among 30–69-year-old persons in three regions of Denmark 1995–2006, standardized for age, sex and income or educational status

<table>
<thead>
<tr>
<th></th>
<th>Copenhagen</th>
<th>Aarhus</th>
<th>Other regions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995–2000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RRT rates and RR</td>
<td>174 (153–195)*</td>
<td>164 (143–185)*</td>
<td>160 (140–180)*</td>
</tr>
<tr>
<td>standardized</td>
<td>1.32 (1.16–1.50)*</td>
<td>1.23 (1.08–1.40)*</td>
<td>1.15 (1.01–1.31)*</td>
</tr>
<tr>
<td>for age and sex</td>
<td>134 (119–150)</td>
<td>135 (119–150)</td>
<td>128 (122–134)</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>1.07 (0.94–1.21)</td>
<td>1.06 (0.93–1.20)</td>
<td>1.00</td>
</tr>
<tr>
<td>RRT rates and RR</td>
<td>181 (158–204)*</td>
<td>173 (151–195)*</td>
<td>165 (143–186)*</td>
</tr>
<tr>
<td>standardized</td>
<td>1.38 (1.21–1.57)*</td>
<td>1.26 (1.10–1.44)*</td>
<td>1.15 (1.01–1.29)*</td>
</tr>
<tr>
<td>for age, sex</td>
<td>145 (127–162)*</td>
<td>154 (136–171)*</td>
<td>134 (128–140)</td>
</tr>
<tr>
<td>and educational status</td>
<td>1.15 (1.02–1.31)*</td>
<td>1.14 (1.01–1.29)*</td>
<td>1.00</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>124 (118–130)</td>
<td>134 (128–140)</td>
<td></td>
</tr>
<tr>
<td>RRT rates and RR</td>
<td>164 (143–185)*</td>
<td>165 (143–186)*</td>
<td>165 (140–180)*</td>
</tr>
<tr>
<td>standardized</td>
<td>1.23 (1.08–1.40)*</td>
<td>1.15 (1.01–1.31)*</td>
<td>1.15 (1.01–1.31)*</td>
</tr>
<tr>
<td>for age, sex</td>
<td>135 (119–150)</td>
<td>145 (128–161)</td>
<td>137 (131–143)</td>
</tr>
<tr>
<td>and income</td>
<td>1.06 (0.93–1.20)</td>
<td>1.06 (0.94–1.20)</td>
<td>1.00</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>128 (122–134)</td>
<td>137 (131–143)</td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05.

For diabetic nephropathy, the standardized rate of patients starting RRT was higher in Copenhagen during 2001–06. Also, the rate of incident chronic RRT patients in the age group 30–69 years resident in Copenhagen was significantly higher compared to other regions even when standardized for differences in income and educational level.

The regional and socio-economic differences in the rates of chronic incident RRT patients may be due to several factors: differences in renal morbidity, sickness behaviour, referral pattern of general practitioners or treatment strategy of nephrology centres.

In accordance with our observations, studies from USA and UK have shown an inverse relationship between socio-economic status and rates of incident RRT patients, with higher rates in the socio-economically disadvantaged group [11–13], while a study from Scotland was inconclusive [17]. In contrast to our study though, these studies used area-level socio-economy as a proxy for individual level socio-economy which might have led to misclassification. In Denmark, socio-economic differences, with higher rates of planned invasive therapy and better adherence to statin treatment after acute myocardial infarction in the socio-economically advantaged, have also been shown despite a universal health care system [9,10]. It is generally taken that educational status is a proxy for health and sickness behaviour. Income might be a proxy for instant resources and mirror the ability of affording renal protective medication.

The rates of incident chronic RRT patients vary enormously within Denmark from 81 to 198 p.m.p. (non-standardized rates) in 2006 [1] and between countries from 125 p.m.p. in Europe (Iceland and Finland (80 p.m.p.) and Germany (213 p.m.p.)) to 360 p.m.p. in USA in 2006 [18,19]. Previous studies have revealed regional differences of incident RRT patients within countries. In some studies, the differences have been ascribed to interracial differences between persons of Western and non-Western origin partly due to socio-economic differences and differences in the prevalence of diabetes and hypertensive end-stage renal disease (ESRD) [3–5,20–24]. The Danish population is relatively homogenous with only 6% in both 1995 and 2006 originating from non-Western populations. Copenhagen had a remarkably higher proportion, 8% in 1995 and 13% in 2006 [14] although standardizing for regional differences in ethnic origin did not change the rates of incident RRT patients (Table 3).

The regional differences in RRT rates seen in Austria, which like Denmark has a homogenous population, have been explained by regional differences in diabetic ESRD [8]. This was also partly true for rates of patients resident in Copenhagen compared to the rest of Denmark during 2001–06. Regional differences due to interracial differences with higher rates of diabetic ESRD among non-western people have also been reported [3–5,22,25–29]. We found a higher rate of incident RRT patients with residence in Copenhagen, which has a higher proportion of immigrants and descendants from non-Western countries compared to the rest of Denmark including Aarhus. But rates did not change when controlled for regional differences of ethnic origin.

Lower socio-economic status, unequal access to health care and poor prevention of progression of kidney failure have also been shown to partly explain interregional differences [20] as well as an inverse relation between distance to dialysis units and RRT patient rates [12,30]. A higher proportion of incident RRT patients among persons with low income seems to partly explain the differences between Copenhagen and the rest of the country for 30–69-year-old patients, though it is important to notice that income can-
not only be interpreted as a cause of RRT but to some extent also as a consequence even when judged by the income in the year 5 years before start of RRT. Higher RRT rates were also seen among individuals with no other education than primary school, but as the proportion of these persons was lower in Copenhagen compared to other regions, this does not explain the differences.

Among indigenous Australians resident in remote areas, higher incident RRT rates were found compared to urban areas [3]. Fan et al. also observed higher rates of new RRT patients among whites and Afro-Americans with residing in rural counties compared to urban areas and in areas with lower physician density as a proxy for health care availability [31]. These findings are in contrast with those of the present study, which might be explained by differences in social security and health care system between Denmark and USA. Analyses of the most and the less urbanized parts of Aarhus County showed higher rates in the most urbanized Aarhus municipality which supports a general practitioner effect in terms of differences in referral pattern for RRT or differences in morbidity more than a centre effect in terms of differences in treatment strategy.

In the general population, regional mortality rates in Copenhagen among 50–79-year-old men and women were higher in all 10-year strata compared to Aarhus County and other regions of Denmark during 1996–2004 [14]. This might indicate that the 50–79-year-old population in Copenhagen is more susceptible compared to Aarhus County and the rest of Denmark. As we do not have information on educational level in the elderly and as most elderly individuals receive a pension, it was not possible to explore whether the higher rates of incident RRT among the elderly in Aarhus and Copenhagen were explained by socio-economic factors. Time to death, the year after start of RRT, standardized for differences in sex and age showed no regional differences, which indicates that there were no regional differences in acceptance of patients considering comorbidity. Long distances or travel time to the nearest dialysis centre may hinder acceptance of dialysis for some older people outside larger city areas in Denmark, whereas those with easier access to outpatient renal clinics and information about dialysis might more often accept chronic RRT.

The rates of elderly patients resident in Aarhus increased markedly over time. This is probably related to the introduction of an assisted automated peritoneal dialysis programme in Aarhus County in the Year 2000. This programme targets frail, mainly elderly, patients characterized by loss of physical independence [32]. Other explanations might be an increase in severe non-diabetic CKD in the elderly and increased referral from general practitioners. Also, rates of 30–69-year-old incident RRT patients increased in Aarhus, indicating that better treatment of patients with CKD with delay of renal failure does not explain the higher rates of elderly patients.

Much debate has been going on whether to start dialysis in CKD patients with increasing age and comorbidity [33–38]. In a recent study, functional status declined in elderly nursing home residents after commencement of RRT [39]. This emphasizes the importance of weighing out life expectancy to quality of life before the acceptance of elderly patients with comorbidity. It might well be that a less restrictive practice of referring patients for chronic RRT is more often applied in patients with resident in the catchment areas of the largest nephrology centres.

This is in agreement with regional variation in incidence of hospital admissions because of myocardial infarction found in Denmark from 2000 to 2004 where age- and sex-standardized rates in Copenhagen and Aarhus were significantly higher compared to the rest of Denmark [40]. Access to dialysis has been unlimited since the early 1990s in Denmark as future trends have been predicted and dialysis capacity continuously dimensioned [41]. In the period from 1995 to 2006, only a single dialysis centre opened and another closed. Therefore, it seems unlikely that differences in incidence rates of RRT patients in regions and over time were related to differences in capacity. On the contrary, the capacity in interventional cardiology was limited until 1993 where enormous improvements were made.

Limitations of the study

A recent validation study of the Danish National Registry on Regular Dialysis and Transplantation showed that the registered type of diabetes was invalid. The overall diagnosis of diabetes was highly reliable, but the proportion of Type 2 diabetics was underestimated. Probably, they were misclassified because of insulin treatment [15]. Consequently, detailed analysis of the relationship between socio-economy and Type 2 diabetes is not possible. Also, a valid and complete registry of all Danish diabetics does not exist and thus comparisons of regional variation in the prevalence of diabetes are impossible. Regional differences in the registration of incident patients in the national RRT registry does not explain the present results as the validation study showed that completeness of incident patient registration was highly acceptable with no regional variation [15]. The rates of incident RRT patients are standardized according to age differences in the studied areas of Denmark which excludes that different proportions of persons aged 70 years or more with corresponding higher rates of incident ESRD patients contribute to the higher rates of incident RRT patients in Copenhagen and Aarhus. Interaction analysis of income and education would have been valuable, but when standardizing for socio-economy, it was not possible to standardize for both at a time to decide the level of influence of either one. This is because it is not possible to create a standard population in Statistics Denmark that is divided into strata according to income and educational level at the same time. Also, we had no information on socio-economy in the elderly but we assume that differences found in patients aged 30–69 years apply to patients aged 70 years or older.

Generally, higher rates of incident chronic RRT in the elderly residing in Copenhagen and Aarhus, the 30–69-year-old persons in Copenhagen and patients with diabetic nephropathy in Copenhagen during 2001–06 as well as income seem to explain most of the regional variation, while educational status was without influence. We assume that
these regional differences might be explained by regional differences in sickness and health behaviour, general practitioner and centre effects.

Preventive measures like reducing the increasing amount of obese persons in Denmark [42] and their increasing risk of Type 2 diabetes and efforts to improve renal protective care in the socially disadvantaged as well as awareness of the ethical issue of life-prolonging treatment in the elderly and those with severe comorbidity are still necessary.

Conclusion

There were marked socio-economic and regional differences in rates of incident chronic RRT patients in Denmark in the period 1995–2006. The rates of incident RRT patients were highest for patients residing in the catchment areas of the two largest nephrology centres and this may be partly explained by a higher frequency of end-stage diabetic nephropathy and a new treatment programme targeting frail, mainly elderly, patients.

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Meropenem removal in critically ill patients undergoing sustained low-efficiency dialysis (SLED)

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Abstract

Background. The purpose of this study was to examine the removal of meropenem during an 8-h sustained low-efficiency dialysis (SLED) session. Using a minimum inhibitory concentration (MIC) = 2 μg/mL as our reference point, we also evaluated the therapeutic adequacy of dosing meropenem as 1 g every 12 h during SLED.

Methods. This was a prospective, open-label study involving 10 intensive care unit patients with renal failure needing SLED. Meropenem was dosed as 1 g every 12 h. To ensure a steady state, the patients received at least two doses prior to the study. SLED was initiated at least 2 h after the last meropenem dose, and each session was at least 8 h. Blood samples were collected during SLED at 0, 2, 4 and 8 h. The 8-h sample approximated the trough level. After centrifuging the samples, the supernatants were analysed by high-performance liquid chromatography.

Results. Most patients were male with a mean age of 63.7 years and a mean weight of 88.9 kg. The SLED prescription was based on each patient’s needs, and the blood flow, dialysate flow and ultrafiltration rates varied by up to 150 mL/min. The mean reduction of plasma meropenem concentration was 79.1 ± 7.3%, and the mean half-life was 3.6 ± 0.8 h during the 8-h SLED. Significantly more meropenem was removed in the first 4 h of SLED compared with the rest of the sessions. The mean plasma trough concentration was 4 ± 1.6 μg/mL.

Conclusions. Meropenem was significantly removed from the blood compartment during SLED. Dosing 1 g of meropenem every 12 h during a typical 8-h SLED session maintains adequate plasma concentrations.

Keywords: dialysis; ICU; meropenem; renal failure

Introduction

Understanding the removal of antibiotics during prolonged dialysis is crucial in the care of intensive care unit (ICU) patients. Meropenem is a synthetic broad spectrum parenteral carbapenem antibiotic that is used in the treatment of severe infections caused by Gram-positive and Gram-negative organisms, including beta-lactamase producers and anaerobes. Achieving and maintaining therapeutic plasma meropenem levels are essential to the survival of critically ill patients with sepsis. The current literature addresses meropenem clearance and dosing regimens in patients receiving intermittent haemodialysis (IHD) and continuous renal replacement therapy (CRRT). Studies have shown that 50% of meropenem in the blood compartment is eliminated by IHD and between 13% and 53% by CRRT [1]. If meropenem is not re-dosed prior to its therapeutic trough level, then patients have windows of susceptibility to the infectious organisms.

Sustained low-efficiency dialysis (SLED), also known as extended daily dialysis (EDD), is a hybrid dialysis technique developed at the University of Arkansas in 1998 that